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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,315	10/24/2003	Takao Abe	AM 100905 P1 (0036119.002)	1495
49598	7590	11/28/2005	EXAMINER BERCH, MARK L	
WILMER CUTLER PICKERING HALE AND DORR LLP / WYETH 60 STATE STREET BOSTON, MA 02109			ART UNIT 1624	PAPER NUMBER

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/693,315

Applicant(s)

ABE ET AL.

Examiner

Mark L. Berch

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-30 and 32-42 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-30, 32-42 are drawn to processes, classified in class 540, subclass 310.
- II. Claim 31, drawn to product, classified in class 540, subclass 310.

Note that this is a modification of the originally presented telephonic restriction.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and process of using the product. The use as claimed cannot be practiced with a materially different product. Since the product is not allowable, restriction is proper between said method of making and method of using. The product claim will be examined along with the elected invention (MPEP § 806.05(i)).

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case The process could be done with the Chloro or iodo derivative. The product can also be used to prepare the 6,6 dibromo compound or the 6-hydroxyalkyl compound or other known derivatives.

Because these inventions are distinct for the reasons given above and the search in the process literature required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

Art Unit: 1624

During a telephone conversation with Hogan on 11/1/2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-30, 32-42. Affirmation of this election must be made by applicant in replying to this Office action. Claim 31 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Note that this subject matter is under prosecution in the parent application.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1624

Claims 1-30, 32-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term "mild base" is indefinite. This limitation is of particular importance because it is the nature of the base which may distinguish the closest prior art from the claims. The specification, page 28, lines 19-20 says, "a mild base such as triethylamine, DMAP, or diisopropyl ethyl amine". This, however, does not define the term, but only gives a few examples. Would the term include inorganic bases such as sodium bicarbonate, sodium methoxide, lithium hydroxide? Would it include organic bases such as tetramethylammonium hydroxide, DABCO, DBU or DBN? The problem is somewhat complicated by the fact that the three examples given (triethylamine, DMAP, and diisopropyl ethyl amine) are all commonly labeled as strong organic bases.
2. The term "low temperature" in claim 1 is similarly indefinite. What is the upper range of this term?
3. The same is true for the "mild temperature" of claim 7.
4. The second choice in claim 6 is not possible. There is no choice of R8 as haloalkylsulfonyl.
5. Formula 7-A in claim 22 is poorly drawn; the two valence lines should not meet; note how this was correctly done for 7-B. Likewise 8-A in claim 9, 9-A in claim 10, 15-A in claim 16, etc.
6. Step (a) in claim 32 makes no sense as written. Dissolving the 6-APA in water and organic solvent will not brominate it. The brominating reagent was left out.

Art Unit: 1624

7. What does “appropriately substituted” mean in the definition of A? How does that phrase modify the claim?
8. 933The R6-R7 combined option is not correct. First, it should say “Together with the N to which these are attached form a ...” Second, the heteroatoms are not optional. There must be at least one heteroatom, i.e., the N of attachment.
9. In claim 19, Z4-Z9 cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.
10. In addition, Z3 cannot be O, S or NR1 in 4-C for the same reason, although it can be on the other two choices.
11. In addition, the Y atoms (bridgehead atoms) cannot be N, as again, that would destroy the aromatic character of the ring.
12. Likewise, in claim 17, Z5-Z8 cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.
13. In addition, the Claim 17, Y2, Y3 and Y4 atoms (bridgehead atoms) cannot be N, as again, that would destroy the aromatic character of the ring.
14. Also, Y2 must be C in 2-B for the same reason.
15. In claim 18, 3-A, Z4 and Z8 cannot be O, S or NR1.
16. Similarly, in 3-B, Z4 and Z5 cannot be O, S or NR1.
17. Also in Claim 18, none of the Y choices can be N.
18. In claim 21, Z4-Z5 cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.
19. In addition, Z3 cannot be in 6-C for the same reason, although it can be on the other two choices.

Art Unit: 1624

20. Y2 in both 6-B and 6-C cannot be N.

21. For the same reasons, Y1 cannot be N in 6-B or 6-A although it can be in 6-C.

22. In claim 23, Z4-Z7 cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.

23. In claim 25, Z1-Z4 and Z6-Z9 in 10-A, and Z1-Z3 and Z4-Z6 in 10-B cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.

24. In claim 26, Z1-Z4 and Z6-Z9 in 11-A, and Z1-Z4 and Z7-Z10 in 10-B, and Z1-Z9 in 11-C cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.

25. In claim 27, Z1-Z4 in 12-A, and Z1-Z3 in 12-B cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring.

26. In claim 28, Z1-Z6 in 13-A, 13-B, and 13-C cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring. This covers all of the Z variables so these choices should be completely removed.

27. In claim 29, Z1-Z8 in 14-A, 14-B, and 14-C cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring. This covers all of the Z variables so these choices should be completely removed.

28. In claim 30, Z1-Z4 in 15-A, and 14-B, and Z1-Z3 in 15-C cannot be O, S or NR1. Such divalent groups cannot be present in a 6-membered aromatic ring. This covers all of the Z variables so these choices should be completely removed.

29. For Y1 and Y2 of 16-B of claim 14, 16-C of claim 15, 1-A in claim 16, 2-A of claim 17, 3-A and 3-B of claim 18, 4-B of claim 19, 5-A and 5-B of claim 20, 6-A of claim 21, 7-B of claim 22, 8-B of claim 23, 10-A of claim 25, 12-A and 12-B of claim 27, 9-B of claim 24,

Art Unit: 1624

- one or the other can be N, but they cannot both be N. If both were N and the ring were aromatic, then one of the N atoms would have 4 bonds. If neither had 4 bonds, then the 5 membered ring would not be aromatic.
30. The same is true for Y1 and Y4 of 4-A in claim 19, 7-A and 7-B of claim 22, 8-A of claim 23, 9-A of claim 24. If both were N, then one of the N atoms would have 4 bonds. If neither had 4 bonds, then the 5 membered ring would not be aromatic.
31. Likewise for Y3 and Y4 of 6-B in claim 21, 7-B in claim 22, and 10-A of claim 25 and 12-A of claim 27. If both were N, then one of the N atoms would have 4 bonds. If neither had 4 bonds, then the 5 membered ring would not be aromatic.
32. For Y2 and Y3 of 8-A in claim 23, neither can be N, as that would destroy the aromatic character of the ring (or give a N with 4 bonds).
33. The same is true for Y3 and Y4 of 8-B in claim 23, 10-A in claim 25, 11-A and 11-B of claim 26, 13-A and 13-B and 13-C of claim 28, 14-A, 14-B and 14-C of claim 29. None of these can be N.
34. And the same is also true of Y1 and Y2 in 10-A of claim 25, 11-A, 11-B and 11-C of claim 26, 12-A of claim 27, 13-A, 13-B and 13-C of claim 28, 14-A, 14-B and 14-C of claim 29, 15-A, and 15-B of claim 30. None of these can be N.
35. This is also true of Y1, Y3 and Y4 of 10B in claim 25. None of these can be N.
36. It is also true of Y1, Y2 and Y3 of 12-B in claim 27. None of these can be N.
37. It is also true of Y1, Y2 and Y4 of 15-C in claim 30. None of these can be N.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1624

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 12, 32-33 and 36-42 rejected under 35 U.S.C. 103(a) as being unpatentable over EP 232966, alone or in view of McOmie or US 4891369, and also in view of 6268393.

In the primary reference, see Step F1 on page 20, along with the detail on page 24, and Formula IC on page 12. A specific example of this type of compound is seen on page 30, example 25. For the second, step, which is the elimination step, applicants use triphenyl phosphine. This is taught by the reference at page 25, line 2. Alternatively, the claim calls for the use of an anhydride; such is seen at examples 30-31, and the use of the acid chloride is seen in ex 32. Although the intermediate compound which applicants call 19, the acylated hydroxy, is not identified in these steps, that m product is presumed to have been made because these are the reagents which make it. Further, example 29 has the intermediate product identified as this reaction was done without the elimination step, showing the acetate. There are two differences.

A. The starting material of the prior art differs from the starting material here in that it has a slightly different protecting group. That is, it has for R4 the protecting group p-methoxybenzyl whereas the claim has p-nitrobenzyl. However, the reference teaches that these are both suitable for the purposes on the invention. The sentence on page 10, lines 48-55 lists both groups. Thus, any compound formed from any of the protecting groups on this list would be obvious variants of the species which appears in the reference.

Further, the secondary references McOmie or US 4891369 teaches the advantage of using the p-nitrobenzyl. One of ordinary skill in the art of synthetic chemistry would know, and McOmie teaches, that the p-nitrobenzyl groups is more stable to acids than is the p-methoxybenzyl group used in the reference, giving a clear motivation for its use. This exemplified in the 4891369 reference, which says (Column 8, lines 13-20) "Especially when the penicillin carboxyl-protecting group represented by R is ... p-nitrobenzyl or the like, the deesterification is advantageously conducted by reduction. When the protecting group is p-methoxybenzyl ... the reaction is advantageously carried out using an acid." Applicants must show unexpected effects arising from the use of one para-substituted benzyl rather than another to overcome this rejection.

B. The aldol condensation is done with a slightly different procedure. EP 232966 uses Lithium amide bases. The current claims use a "mild base" (whatever that is), plus a Lewis base, e.g. Mg salt. The last reference teaches exactly such an equivalence in an aldol reaction. In 6268393, see paragraph bridging columns 22-23, which states that in staead of LDA (lithium diethyl amide), other bases such as amines can be used; and MgBr₂ appears as an auxiliary at column 23, line 4. A similar teaching appears as the first full paragraph in Column 27. This is the exact variation that applicants employ. Thus, such a variation is obvious. Note that the diisopropyl ethyl amine which is named in claim 4 is named in this reference as well.

With regard to the chilling of claim 5, see primary reference, line 22. The heterocycles of claim 12 are provided for at page 8, lines 1-23.

With regard to claims 41-42, the same applies, except that point A is not a difference, since these claims, unlike claim 1, do permit the p-methoxybenzyl group.

Art Unit: 1624

With regard to claims 32-33 and 36-40, these additionally provide for the synthesis of the penem 16. This is also shown in the reference, basically as Process B, using Route C at the end. The first part of step (a) has been ignored, as it makes no sense (see above). The second part is seen at page 13, lines 25-26. Step (b), corresponds to A1 of the reference and appears as Example 2c. Steps c) and d) correspond to step B1 and are seen in Example 2d. Step e) is Step B2 of the reference and appears at page 21, last 4 lines. Step f) corresponds to Steps C1-C2-A9 and appears at page 22, lines 10-15. Note in this regard that claim 34 is not rejected. IF the text of the second line of claim 34 were inserted into the first part of step (a) of claim 32, that would overcome the rejection.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-30, 32-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31, 33-40 of copending Application No. 10427666. Although the conflicting claims are not identical, they are not patentably distinct from each other because this is essentially the same process involved as is present in the parent case.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art Unit: 1624

Claims 1-30, 32-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and others of copending Application No. 10427427. Although the conflicting claims are not identical, they are not patentably distinct from each other because this is essentially the process for making the compounds of 10427427. There is ordinarily no patentable distinction between compositions of matter and methods. Hence, in the absence of a Terminal Disclaimer, an obviousness-type Double Patenting rejection may be made. See *In re Boylan*, 157 USPQ 370, Ex parte MacAdams, 206 USPQ 445; *Geneva Pharmaceuticals Inc. v. GlaxoSmithKline PLC*, 68 USPQ2d 1865 (CA FC 2003).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Specification

The abstract is objected to. It states that there is a process, but does not state what the process actually consists of.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663.

The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark L. Berch
Primary Examiner
Art Unit 1624

11/22/05